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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/791,648	03/02/2004	James P. Elia	1000-10-C5	3064

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EXAMINER	
GAMETT, DANIEL C	
ART UNIT	PAPER NUMBER
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/791,648	ELIA, JAMES P.	
	Examiner	Art Unit	
	Daniel C. Gamett, PhD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *159-223* is/are pending in the application.

4a) Of the above claim(s) *168-187 and 200-223* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *159-167 and 188-199* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/02/2004 11/24/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1647.

2. Claims 159-223 are pending in this application.

3. Applicant's election without traverse of claims 159-167 and 188-199 in the reply filed on 11/24/2006 is acknowledged. Claims 168-187 and 200-223 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/24/2006.

4. Claims 159-167 and 188-199 are under examination insofar as they read upon a method of treating arthritis comprising administering cells.

Priority

5. This application is a continuation of application Ser. No. 10/179,589 filed Jun. 25, 2002, which in turn is a continuation-in-part of application Ser. No. 09/064,000 filed Apr. 21, 1998. The conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). Based on the information given by applicant and an inspection

of the patent applications, the examiner has concluded that the disclosure of the prior-filed application, Application No. 09/064,000, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Application 09064000 does not provide an enabling disclosure for methods of treating arthritis or avascular necrosis comprising administration of cells, and therefore this earlier applications does not comply with the requirements of the first paragraph of 35 U.S.C. 112 with respect to claims 159-167 and 188-199. Accordingly, the subject matter defined in claims 159-167 and 188-199 has an effective filing date of 06/05/2002, the earliest date on which this disclosure was filed.

6. Should the applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to 06/05/2002 which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled for prior to 06/05/2002.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 164 and 196 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "blood stem cell" is not precisely defined either in

the art or in the instant specification. It might refer to hematopoietic stem cells, which are capable of reconstituting the cells of blood. Alternatively, the term may refer to any kind of stem cell that might be found in the blood; cells that can give rise to endothelial, connective, and neural cells have been alleged. The specification does not provide guidance as to the intended scope of the term "blood stem cell".

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 159-167 and 188-199 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for of treating avascular necrosis by administration of bone marrow cells, osteogenic precursor cells or mesenchymal stem cells, does not reasonably provide enablement for treatment of all forms of arthritis with all kinds of stem cells, cloned cells, or cultured cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The courts have interpreted the first paragraph of 35 U.S.C. 112 to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re

Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986), and are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

a. *The nature of the invention:* The instant claims are drawn to methods for treating arthritis comprising inserting cells at a desired location in a human patient.

b. *The breadth of the claims:* The disease to be treated is any form of arthritis (claims 159-167) or "arthritis of an avascular necrosis nature" (claims 188-199). The cells to be administered are described variously as any cell (claim 161), stem cell (162), bone marrow stem cell (claim 163), blood stem cell (claim 164), germinal cell (claim 165), cloned cell (claim 166) and cultured cell (claim 167).

c. *The state of the prior art and the predictability or lack thereof in the art:* Joel Boyd, MD, an orthopedic surgeon at TRIA Orthopaedic Research Institute, Minneapolis, Minnesota, is quoted in an April 25, 2006 announcement (see Ref. AI in the IDS filed 11/24/2006) that, "The ability to give patients a simple injection into the knee that could restore the meniscus and prevent the inevitable progression to osteoarthritis *would be* a significant advancement in the treatment of knee pain" (emphasis added). This indicates

that nearly 4 years after the instant disclosure was filed, considerable uncertainty remained in the field of cellular therapy for osteoarthritis. The prior art provides teaching of treating avascular necrosis by administration of bone marrow cells, osteogenic precursor cells or mesenchymal stem cells (U.S. Patent 5,827,289, see below). The prior art provides teaching of treating osteoarthritis by administration of mesenchymal stem cells (by U.S. Patent 6835377, see below). The general term "arthritis" includes over 100 diseases (definition from Biology-Text.com). The art does not teach that any cell, cloned cell, cultured cell, or any kind of stem cell other than the aforementioned cells can be used for treatment of arthritis of any kind.

d. The amount of direction or guidance present and the presence or absence of working examples: Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991). The specification does not incorporate or cite any references that teach treatment of arthritis or avascular necrosis by administration of cells. The specification provides no examples of treatment of arthritis or avascular necrosis by administration of cells. Even the concept of using cells to treat arthritis or avascular necrosis can only be pieced together from disparate sections of the specification. The following teaching on page 4 might be taken to suggest (but this is not clear) that cells can be used in the methods to be disclosed, "As used herein, the term growth factor encompasses compositions and living organisms which promote the growth of hard tissue, such as bone, or soft tissue, in the body of a patient. The compositions include organic and inorganic matter. The compositions can be genetically produced or manipulated. The living organisms can be bacteria, viruses, or

any other living organism which promote tissue growth." Specific teaching about avascular necrosis and arthritis is found at page 28, line 12 to page 29, line 14. This section teaches that, "Avascular necrosis can be corrected with the insertion of a gene(s) and/or growth factor or other genetic material in the body... VEGF or BMP genes, or VEFG or BMP growth factors produced by VEFG or BMP genes, respectively, or any other desired genetic based material can be inserted to regrow blood vessels and/or bone...Insertion of a growth factor (or its gene counterpart) in the body can be utilized to prevent and/or reduce inflammation. Growth factors control cell migration. As such, they can be powerful cell inhibitors to prevent inflammatory cells from migrating into an area. Such an application has major usefulness in the treatment of arthritis or other autoimmune or inflammatory diseases." Thus, the specification clearly directs the skilled artisan toward the use of polypeptide growth factors, not whole cells. Furthermore, even these teachings are general and prophetic—no working examples are provided. **Therefore, it is clear that the enabled scope described in this rejection is provided entirely by that which is known in the prior art.**

e. *The quantity of experimentation needed:* The development of cellular therapies for arthritis is a relatively new field. It is theoretically possible that cells other than bone marrow cells, osteogenic precursor cells, or mesenchymal stem cells might eventually be used to treat osteoarthritis or avascular necrosis. It may eventually be possible to treat other forms of arthritis with cellular therapies. The instant specification does not contribute any technical or conceptual advancement toward these goals beyond that which was already known in the art and offers instead mere speculation as to the

possibilities. The courts have stated that patent protection is granted in return for an enabling disclosure, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute an enabling disclosure. Reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. See *Genentech v. Novo Nordisk A/S* (CAFC) 42 USPQ2d 1001 (1997).

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 159, 160, 188-192 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 5,827,289, issued October 7, 1998. The instant claims are drawn to methods for treating arthritis comprising inserting a growth factor at a desired location in a human patient. Applicant's elected invention is drawn to a method of treating arthritis comprising administering cells. Even if it is argued that the lexicon of the instant application permits the inclusion of "cell" within the generic term "growth factor", the standard meaning of "growth factor" is also

encompassed. The '289 patent teaches a method of delivering therapeutic substances, including growth factors, into the femoral head for the treatment of avascular necrosis (see Fig. 20; column 18, lines 20-64). The factors taught in the '289 patent include BMP, FGF, and TGFβ, agents known to promote bone growth, angiogenesis, and anti-inflammatory activities (column 19, lines 37-44). These teachings anticipate all the limitations of the instant claims, including the patient population, agents to be administered, location of administration, and expected results. This rejection could be overcome by amending the claims to recite "cell" or "cells" instead of "growth factor".

13. Claims 159-164, 167, 188-196 and 199 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 6,300,127, issued October 9, 2001. The '127 patent teaches injection of *ex vivo* transfected (cultured as in instant claims 167 and 199) bone marrow cells, osteogenic precursor cells or mesenchymal stem cells for inducing new bone formation in avascular necrosis of the hip or knee (column 4, lines 42-58). These teachings anticipate all the limitations of the instant claims, including the patient population, agents to be administered, location of administration, and expected results.

14. Claims 159-163 and 167 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 6835377, filed May 13, 1998. The '377 patent teaches a method for regenerating articular cartilage defects in a host in need thereof, comprising administering to said host cultured human mesenchymal stem cells (see claim 1). The method is for repair of cartilage damaged as part of the degenerative effects of osteoarthritis (see Abstract). These teachings explicitly or inherently anticipate all the limitations of the instant claims, including the patient population, agents to be administered, location of administration, and expected results.

Conclusion

15. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C Gamett, Ph.D., whose telephone number is 571 272 1853. The examiner can normally be reached on M-F, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571 272 0961. The fax phone number for the organization where this application or proceeding is assigned is 571 273 8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DCG
Art Unit 1647
24 January 2007

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